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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/770,102	01/25/2001	Roger Craig	10069/1062	5353

29933 7590 04/26/2004

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EXAMINER

COUNTS, GARY W

ART UNIT PAPER NUMBER

1641

DATE MAILED: 04/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/770,102	<b>Applicant(s)</b> CRAIG, ROGER	
	<b>Examiner</b> Gary W. Counts	<b>Art Unit</b> 1641	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 January 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-5, 7-13, 27, 28, 32-34, 51 and 52 is/are pending in the application.
- 4a) Of the above claim(s) 35-50 and 55-78 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-13, 27, 28, 30, 32-34, 51 and 52 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### **Status of the claims**

The amendment filed January 30, 2004 is acknowledged and has been entered.

### ***Election/Restrictions***

1. Newly submitted claims 77 and 78 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Claims 77 and 78 the addition or removal of the moiety promotes dissociation and further requires detecting dissociation and the originally filed claims do not require these limitations. (see also reasons stated in the restriction requirement filed June 18, 2002).

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 77 and 78 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

### ***Claim Objections***

2. Claims 2-4, 7-9, 11, 27, 28, 30, 32-34, 51 and 52 are objected to because of the following informalities: Amended claims 2-4, 7-9, 11, 27, 28, 30, 32-34, 51 and 52 depend from non-elected invention. It is recommended to delete the dependency from the non-elected claims (i.e. it is recommended to delete the dependency from claims 77 and 78).

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-5, 7-13, 27, 28, 30, 32-34, 51 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: immobilization of the binding partner polypeptides and a wash step. Without the above steps the instantly recited claims do not work because the detector molecule binds to the tag binding partner and regardless if enzyme activity occurs the detection molecule will bind to the tag binding partner and thus a positive signal will be detected. Further, a wash step would have to be performed after the addition of the detection molecule to determine if binding of the detection molecule has occurred and also to remove excess detection molecule.

Claims 1 and 51 are vague and indefinite because it is unclear how applicant can detect binding between the tagged binding partner polypeptides and the binding partner polypeptides by the addition of the detector molecule. The detector molecule as recited binds to the tagged binding partner and regardless if the tagged binding partner binds the binding partner polypeptide or not the detector molecule will bind to the tagged

binding partner and thus a positive signal will always be detected. Claims 1 and 51 as instantly recited will not work.

Claims 1, part (ii) the recitation "correspond to said tagged binding partner polypeptides" is vague and indefinite. How does the binding partner polypeptide correspond to the tagged binding partner polypeptide. Does it comprise similar sequences, does it bind to the tagged binding partner polypeptide or is there another binding partner polypeptide? See also deficiency found in claim 51.

Claim 1 is vague and indefinite because it is unclear if the moiety is in the mixture floating around and the enzyme causes it to attach to the polypeptide or is the moiety part of the polypeptide to begin with and the enzyme causes a conformational change or release of the moiety. Please clarify.

Claim 5 is vague and indefinite because it is unclear how the rate of diffusion of the fluorescent molecule is monitored. It is unclear what media the fluorescent molecule is in. Is it in a solution or a gel? Further, the instantly recited claims could be performed in a test tube and if so it is unclear if a diffusion rate could be performed in this environment. Please clarify.

Claim 12 is vague and indefinite because as recited the binding partner would comprise a fluorescent molecule, the tagged binding partner would comprise a fluorescent molecule and the detector molecule would comprise a reporter molecule. There would be labels and it is unclear how detection would be carried out with three labels. The specification provides for FRET which uses two labels (p. 65) and

embodiments in which a single label can be used. However, the specification does not provide guidance for three labels as recited. Please clarify.

***Claim Rejections - 35 USC § 102***

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-4, 7, 9, 10, 11, 13, 28 and 32-34 are rejected under 35 U.S.C. 102(e) as being anticipated by Heroux et al (US 6,312,896).

Heroux et al disclose methods for measuring the activity of enzyme. Heroux et al disclose combining an immobilized substrate and a substrate molecule with an enzyme. Heroux et al discloses that the enzyme causes a change in the substrate molecule (for example phosphorylation of a protein) that induces the substrate to bind to a second molecule (col 11, lines 1-62). Heroux et al disclose that the substrates can be polypeptides and that these polypeptides can contain natural and unnatural units (col 12, lines 1-32). Heroux et al disclose that the substrates can be labeled (tagged) with ECL labels. Heroux et al disclose an embodiment in which an immobilized substrate (binding partner) is combined with two tagged substrates and an enzyme (one tagged substrate and one detector molecule). Heroux et al disclose that the second tagged substrate (detector molecule) binds with the first tagged substrate (tagged binding

partner) (See Figure 6d). Heroux et al disclose that the invention can be used to assay an enzyme inhibitor (modulator) and/or to measure the inhibitory ability of test compound (col 14). Heroux et al disclose that FRET assays can be used to study the binding events (col 19). Heroux et al disclose that the detectable label can be a radioisotope (radioactive molecule).

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heroux et al in view of Levin et al (US 2002/0197696).

See above for teachings of Heroux et al.

Heroux et al differ from the instant invention in failing to teach monitoring the rate of diffusion of the fluorescent molecule.

Levin et al disclose Fluorescence Correlation Spectroscopy (FCS), which measure the average diffusion rate of a fluorescent molecule within a small sample volume. Levin et al disclose that FCS can be applied to protein-ligand interaction (p. 13, paragraph 0143).

It would have been obvious to one of ordinary skill in the art to incorporate Fluorescence Correlation Spectroscopy as taught by Levin et al into the modified method of Blau et al because Levin et al teaches that FCS provides for the average diffusion rate of a fluorescent molecule within a small sample volume and that it can be applied to protein-ligand interactions.

10. Claims 8, 27 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heroux et al in view of Colyer et al (WO 99/11774).

See above for teachings of Heroux et al.

Heroux et al differ from the instant invention in failing to specifically teach the one or more sites comprise a sequence, which directs modification by an enzyme such as kinase or phosphatase.

Colyer et al disclose a method for monitoring the activity of an enzyme comprising monitoring the addition or removal of a moiety (p. 15). Colyer et al disclose that the site contains an amino acid sequence, which is recognized by a post-translational modifying enzyme. Colyer et al also disclose that the modifying enzyme can be a kinase or phosphatase (p. 17). Colyer et al teaches that the use of such enzymes provides for efficient means of monitoring of post-translational modification of a protein (p. 5).



It would have been obvious to one of ordinary skill in the art to the use of enzymes as taught by Colyer et al into the method of Heroux et al because Heroux et al specifically teaches the enzyme causes a change in the substrate molecule (for example phosphorylation of a protein) (col 11, lines 1-62) and Colyer et al teaches that the use of such enzymes provides for efficient means of monitoring of post-translational modification of a protein.

With respect to the detector molecule being pre-bound to the one or more tagged binding partner polypeptides as recited in the instant claims. It would have been obvious to one of ordinary skill in the art to premix the detector molecule and the tagged binding partner before mixing with the binding partner polypeptide because premixing would allow for a longer incubation and would also allow for incubation without the presence of interfering substances.

11. Claims 51 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heroux et al in view of Colyer et al (WO/99/11774).

See above for teachings of Heroux et al.

Heroux et al differ from the instant invention in failing to specifically teach detecting binding of the binding partner polypeptides and the tagged binding partner polypeptides in both the presence and absence of candidate modulators.

Colyer et al disclose a method for monitoring the activity of an enzyme comprising monitoring the addition or removal of a moiety (p 15). Colyer et al disclose methods for screening a candidate modulator (p. 17-18). Colyer et al also teach detecting binding of the binding partner in both the presence and absence of a

candidate modulator (p. 18). Coyler et al discloses this provides for an efficient means of monitoring and/or modulating post-translational modification (p 5).

It would have been obvious to one of ordinary skill in the art to perform the method of Heroux et al in both the presence and absence of a candidate modulate as taught by Coyler et al because Heroux et al specifically teaches their method can be used to assay an enzyme inhibitor (modulator) and/or to measure the inhibitory ability of test compound and further because Coyler shows that detecting the binding or the binding partner in both the presence and absence of a candidate modulator provides for an efficient means of monitoring and/or modulating post-translational modification.

### ***Response to Arguments***

12. Applicant's arguments, see amendment, filed 1/30/2004, with respect to the rejection(s) of claim(s) 1, 3, 4, 7, 8, 27, 28, 30, 32-34 and 51 rejected under 103(a) as obvious over Blau et al. (WO 98/44350) in view of Colyer (WO 99/11774) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Heroux et al (US 6,312,896).

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.


Art Unit: 1641

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Gary Counts  
Examiner  
Art Unit 1641  
April 22, 2004



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04/22/04